Remarks and Arguments

Claims 1-17 were presented for examination. Claims 1, 8 and 12 have been amended. Claim 13-17 have been withdrawn from consideration in response to a telephone election.

Applicants affirm the election of claims 1-12 as provisionally elected in a telephone conversation with the examiner on June 22, 2007.

Claim 12 has been objected to for reciting "a pipetting robot" in line 3, since a pipetting robot had already been recited in parent claim 11. In response, claim 12 has been amended to recite "the pipetting robot", in line 3, as suggested by the examiner.

Claims 1-12 have been rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the enablement requirement. Specifically, the examiner comments that claim 1 recites a method that comprises multidimensional separation and specifically describes how a first dimension of separation is achieved. However, the examiner asserts that the claim does not explicitly recite how subsequent dimensions are separated to produce sub-fractions. The examiner considers the recitation of "two or more separation generations with different separating dimensions are used to successively separate the respective fractions into multiple discrete sub-fractions" to be indefinite for purposes of describing the separation of subsequent generations.

The specification clearly describes separation in multiple dimensions. See, for example, page 9, line 20-page 10, line 12. Thus, it appears that the examiner's rejection is the result of indefiniteness of the claim wording. In response, claim 1 has been amended to recite, in lines 8-12, "...the separated biosubstances in each discrete fraction are further successively separated into discrete sub fractions using a second fractionating binding on solid surfaces or a second fractionating dissolution from a surface through specially adjusted solvents." which clearly reads onto the original specification. Accordingly, the rejection under 35 U.S.C. §112, first paragraph, is hereby traversed.

Claim 8 has been rejected under 35 U.S.C. §112, second paragraph, because it recites a step of performing enzymatic digestion, but the examiner considers it unclear when this step is performed relative to the other recited steps. In response, claim 8 has been amended to recite that the enzymatic digestion takes place "after the separation

into sub fractions and before the mass spectrometric analysis." Thus, amended claim 8 now specifies when the enzymatic digestion takes place.

Claims 1-3, 11 and 12 have been rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,537,432 (Schneider.) The examiner comments that the Schneider reference discloses multi-dimensional separation with the first dimension achieved by affinity chromatography.

The Schneider reference discloses protein separation by electrophoresis with a single pre-separation by affinity chromatography. If the first separation dimension is taken to be separation by affinity chromatography, then it is clear that any remaining separations are performed by electrophoresis and not by binding on solid surfaces or solvent-based dissolution separation techniques. Claim 1 has been amended to recite that fractions resulting from the first separation are "successively separated into discrete sub fractions using a second fractionating binding on solid surfaces or a second fractionating dissolution from a surface through specially adjusted solvents" Such a step is not disclosed in the Schneider reference. Thus, claim 1 patentably distinguishes over the Schneider reference. Claims 2-3 and 11-12 are dependent on claim 1 and incorporate the limitations thereof. Therefore, they distinguish over the cited reference in the same manner as claim 1.

Claims 1-4, 11 and 12 have been rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,240,602 (Hammen.) The examiner comments that the Hammen reference discloses the separation of at least one substance from a mixture of substances.

The Hammen reference discloses a material suitable for affinity chromatography and discloses using that material in wells of a microtiter plate. However, only one separation is disclosed. Amended claim 1 clearly recites that at least two separations are performed both with either affinity binding to a solid surface of solvent-based dissolution. Thus, claim 1 patentably distinguishes over the Hammen reference. Claims 2-4 and 11-12 are dependent on claim 1 and incorporate the limitations thereof. Therefore, they distinguish over the cited reference in the same manner as claim 1.

Claims 1-3, 7, 11 and 12 have been rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,561,045 (Dorval.) The examiner comments that the

Dorval reference discloses the separation of at least one substance from a mixture of substances using immobilization of an antibody on a substrate and then binding of the substance to the antibody.

The Dorval reference discloses detection of analytes by binding to an immune agent. However, again, only a single binding and thus, a single separation, is disclosed. As amended claim 1 clearly recites that at least two separations are performed both with either affinity binding to a solid surface of solvent-based dissolution, it patentably distinguishes over the Dorval reference. Claims 2-3, 7 and 11-12 are dependent on claim 1 and incorporate the limitations thereof. Therefore, they distinguish over the cited reference in the same manner as claim 1.

Claims 1, 2, 8, 11 and 12 have been rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent Publication No. 2002/0045204 (Nordhoff.) The examiner comments that the Nordhoff reference discloses multidimensional separation of a protein mixture and then enzymatic digestion of the proteins prior to mass spectrometric analysis.

The Nordhoff reference discloses digesting proteins in gel pieces, removing the resulting peptides via centrifuging and then adsorbing the peptides on specially prepared surfaces, but it does not disclose generation of sub-fractions beyond the initial adsorption separation step. Amended claim 1, in reciting a second separation step, patentably distinguishes over the Nordhoff reference in the same manner that it distinguishes over the Hammen and Dorval references. Claims 2, 8 and 11-12 are dependent on claim 1 and incorporate the limitations thereof. Therefore, they distinguish over the cited reference in the same manner as claim 1.

Claims 9 and 10 have been rejected under 35 U.S.C. §103(a) as obvious over the Schneider reference in view of U.S. Patent No. 5,240,604 (Cortes.) The examiner comments that the Schneider reference discloses all of the claimed limitations with the exception that it does not disclose the use of exclusion chromatography. However, the examiner asserts that the Cortes reference discloses a chromatographic multidimensional separation system wherein the first separation dimension is achieved by size-exclusion chromatography. The examiner concludes that it would have been

obvious to combine the teachings of Schneider and Cortes in order to separate the proteins according to size.

The Cortes reference discloses size exclusion chromatography, however, its combination with Schneider does not add to Schneider the multi-dimensional fractionation by means of affinity binding to a solid surface or solvent-based dissolution that is discussed above. Consequently, the combination of Schneider and Cortes does not teach or suggest the invention recited in claim 1. Since claims 9 and 10 are dependent on claim 1 and incorporate the limitations thereof, they distinguish over the cited reference in the same manner as claim 1.

Claims 5 and 6 have been rejected under 35 U.S.C. §103(a) as obvious over the Hammen reference in view of U.S. Patent No. 5,867,918 (Wainwright.) The examiner comments that the Hammen reference discloses all of the claimed limitations with the exception that it does not disclose the use of magnetic spheres. The examiner asserts that the Wainwright reference discloses the use of magnetic spheres to perform a separation and concludes that it would have been obvious to perform a separation using the magnetic spheres in order to facilitate collection of an isolated species.

The Wainwright reference discloses the use of coated microspheres, but does not supply a disclosure missing in the Hammen reference relating to a second separation performed via affinity binding or solvent-based dissolution as recited in claim 1 and as discussed above. Since claims 5 and 6 are dependent on claim 1 and incorporate the limitations thereof, they distinguish over the cited reference in the same manner as claim 1.

In light of the forgoing amendments and remarks, this application is now believed in condition for allowance and a notice of allowance is earnestly solicited. If the examiner has any further questions regarding this amendment, he is invited to call

applicants' attorney at the number listed below. The examiner is hereby authorized to charge any fees or direct any payment under 37 C.F.R. §§1.17, 1.16 to Deposit Account number 50-3969.

Respectfully submitted

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